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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,465	10/19/2000	Peter Kufer	147-199P	3425

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	PAPER NUMBER
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	12/29/2006	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 12/29/2006.

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mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	09/554,465	KUFER ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 19-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24 and 32-35* is/are allowed.

6)☒ Claim(s) *22-23, 25-31, 39-40,* is/are rejected.

7)☒ Claim(s) *1-17,19,36-38,41 and 42* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 10/24/06
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and Dr. Raum affidavit filed on 10/24/2006 have been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claim 18 is cancelled.
2. Claims 38-42 are added.
3. Claims 1-17, 19-42 are under examination.

Claim Rejections - 35 USC § 112

Enablement

CDR Binding Region

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-23, 25-31 and 39-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the

amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The instant invention directs to a method of identifying at least one epitope binding domain capable of binding to a predetermined epitope. The said method comprise using phage library display system having a N-terminal block domain linked to V_H-V_L (recombinant polypeptide) connecting its C-terminal to an anchoring CT domain in identifying potential binding domain on the V_H-V_L.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. (See Paul, Fundamental Immunology, (textbook), 1999, under the heading "Immunoglobulins: Structure and Function, , pp. 37, 43, 58, 59; Janeway et al. eds. Immunobiology, third edition, section 3-6 and 3-7). It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

With respect to claim language "at least three of the complementary determining regions from SEQ ID 61, 63, 65, 67, 69, 71, 73, 75 and 77, the selection would impose undue experimentation problem. Applicant had submitted affidavit and disclosed the detailed of CDR H/L 1-3 regions on each SEQ ID (See affidavit page 6, Table). However, choosing at least three from the pool of the SEQ IDs, and each CDR H or CDR 1 fragment may also involve conformation change, would impose undue experimentation. It is because antigen-antibody binding is a delicate relationship requiring "latch-lock"

perfect fitting. Randomly selecting any three of the regions, ranging from CDR H (1-3) of any SEQ ID to CDR L (1-3) of any SEQ ID, would not meet this "latch-lock" fitting relationship.

Furthermore, there no antigen or predetermined epitope is recited in claim 22 with respect to the binding to the CDR. It is noted claim 22 depends on claim 1 which is a method of identifying at least one epitope binding domain capable of binding to a predetermined epitope. This method would identify a set of recombinant polypeptide having the target epitope binding domain for the specific predetermined epitope. In claim 22, applicant recites a series of known CDR regions selected from SEQ ID 61, 63, 65, 67, 69, 71, 73, 75 and 77. The selected binding domain is known, yet there is no information with respect to the "*predetermined*" epitope (emphasis added). The selected binding domain comprise the selected SEQ ID cannot bind to ANY predetermined epitope. Without further clarification with regard to the predetermined epitope, it would inevitably impose undue burden to one artisan in the field to perform the recited method.

In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-17, 19-23, 25-31, 36-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, it is not clear whether the "epitope binding domain" is within the recombinant polypeptide. Similarly claim 21 shares the same problem.

With respect to claim 1, the recited method needs to place the predetermined epitope into the display system.

With respect to claim 1, the preamble is to identify "epitope binding domain" capable of binding to a predetermined epitope. However, the end of the method merely recites the identified "recombinant polypeptides". It is not clear whether this identified recombinant polypeptide is the epitope binding domain.

With respect to claim 22, line 2 "obtainable" is vague and indefinite. The wording should be "identified" consistent with claim 1 since claim 1 is to identify the suitable epitope binding domain. Similarly, claim 30 shares the same problem.

With respect to claim 32, the recited language "set forth in" imply "fragments". It is not clear about the metes and bounds of the amino acid sequence. Similarly, claims 33 and 35 shares the same problem.

Response to Applicant's Arguments

Enablement

Applicant's arguments with respect to the enablement rejection together with the affidavit filed by Dr. Raum have been considered. Dr. Raum's affidavit reviews the fundamental knowledge of the CDR in the antibody. Dr. Raum also present detailed information with respect to the CDR sequence, including SEQ ID No. 61, 63, 65, 67, 69, 71, 73, 75 and 77. Applicant has clearly indicated each SEQ ID encompasses six CDR locations, namely CDR H1-3 and CDR L1-3.

Examiner found the arguments persuasive, in part.

Although the disclosed information could provide one ordinary skill in the art the information with respect to the CDR of the antibody, nevertheless claim 22 still suffers the shortage of lack of a definite "predetermined epitope" corresponding to the selected SEQ ID Nos of CDR as discussed in this Office Action. Furthermore, the language "at least three" also imposes undue experimentation under enablement requirement.

Allowable Subject Matter

5. Claims 17, 19-23, 25-31, 36-41 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

6. Claims 24, 32-35 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jacob Cheu
Examiner
Art Unit 1641

December 20, 2006

LONG V. LE 12/22/06
SUPERVISORY PATENT EXAMINER
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